

CLAIMS

1. A method for producing a multi-component protein, said method comprising:

5 (a) introducing a first nucleotide sequence into a first cell, wherein the first nucleotide sequence encodes a first component of the multi-component protein;

(b) introducing a second nucleotide sequence into a second cell, wherein the second nucleotide sequence encodes a second component of the multi-component protein;

10 (c) optionally, repeating step (b) for each remaining component of the multi-component protein; and

(d) fusing cells produced from steps (a)-(c) to form a hybrid cell, wherein the hybrid cell expresses the multi-component protein.

15 2. The method of claim 1, further comprising:

(e) culturing the hybrid cells so as to express the multi-component protein; and

(f) recovering the multi-component protein from the hybrid cell culture.

20 3. The method of claim 1, wherein said first cells and said second cells are selected from the group consisting of a mammalian cell, a myeloma cell, and a non-lymphoid cell.

4. The multi-component protein of claim 1, wherein
25 said protein is an antibody.

5. A method for producing an antibody, said method comprising:

(a) introducing a nucleotide sequence encoding a desired heavy chain into a first cell;

5 (b) introducing a nucleotide sequence encoding a desired light chain into a second cell; and

(c) fusing the first and second cells to form a hybrid cell, wherein the hybrid cell expresses the antibody.

6. The method of claim 5, further comprising:

10 (e) culturing the hybrid cells so as to express the multi-component protein; and

(f) recovering the multi-component protein from the hybrid cell culture.

7. The method of claim 5, wherein said nucleotide
15 sequence is obtained from a B-cell or a hybridoma cell, wherein said B-cell or hybridoma cell produce an antibody.

8. The method of claim 5, wherein the first cell expresses an irrelevant light chain and expresses the desired heavy chain prior to fusion with the second cell.

20 9. The method of claim 5, wherein expression of the desired heavy chain by the first cell is determined by ELISA analysis of lysate from the first cell.

10. The method of claim 5, wherein the antibody is expressed only after fusion of said first and second cells.

25 11. The method of claim 5, wherein the first cell expressing the desired heavy chain is further selected for one or more desirable characteristics.

12. The method of claim 5, wherein both the second cell expressing the desired light chain and the first cell expressing the desired heavy chain are each further selected for one or more desirable characteristics.

5 13. The method of claim 12, wherein said desirable characteristic is selected from the group consisting of high production rate of the heavy chain and high production rate of light chain.

10 14. A method for producing an antibody, said method comprising:

 (a) introducing a nucleotide sequence encoding a desired heavy chain into a first cell, wherein the first cell expresses an irrelevant light chain;

15 (b) introducing a nucleotide sequence encoding a desired light chain into a second cell; and

 (c) fusing the first and second cells to form a hybrid cell, wherein the hybrid cell expresses the antibody.

15 15. The method of claim 14, further comprising:

20 (e) culturing the hybrid cells so as to express the multi-component protein; and

 (f) recovering the multi-component protein from the hybrid cell culture.

16. The method of claim 14, wherein said irrelevant light chain is present in an episomal vector.

25 17. A multi-component protein produced by the method of claim 1.

18. An antibody produced by the method of claim 5.

19. A antibody produced by the method of claim 14.

20. A method for screening for successful fusion of a first cell containing a first nucleotide sequence encoding a desired antibody heavy chain and a second cell containing
5 a second nucleotide sequence encoding a desired antibody light chain, comprising:

including a nucleotide sequence encoding a first marker gene in the first cell;

including a nucleotide sequence encoding a second
10 marker gene in the second cell;

fusing the first cell and the second cell under fuseogenic conditions to produce a fused cell; and

assaying for the presence of the first and second marker genes in the fused cell, wherein detection of the
15 presence of the first and second marker genes in the fused cell indicates a successful fusion.

21. The method of claim 20, wherein the first marker gene is independently selected from the group consisting of the hygromycin resistance gene, the neomycin
20 resistance gene, the hypoxanthine phosphoribosyl transferase gene, the dihydrofolate reductase gene, and the LacZ reporter gene and the second marker gene is independently selected from the group consisting of the hygromycin resistance gene, the neomycin resistance gene, the
25 hypoxanthine phosphoribosyl transferase gene, the dihydrofolate reductase gene, and the LacZ reporter gene.

22. The method of claim 20, wherein the first marker gene is the hypoxanthine phosphoribosyl transferase and the second marker gene is the LacZ reporter gene.

23. The method of claim 20, wherein the first marker gene is the LacZ reporter gene and the second marker gene is the hypoxanthine phosphoribosyl transferase gene.